REMARKS

Applicants wish to thank the Examiner for the review of the present application. Claims 1 and 13 have been amended. Claims 1 and 6-22 are currently pending in the application.

35 U.S.C. §112

Claims 1 and 6-22 are rejected under 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the office action states that it is unclear how to determine parameters from an image, as directed in claims 1 and 16.

Applicants contend that there is direction throughout the specification of how to determine parameters from an image, but specifically direct the examiner's attention to paragraphs 67-72, wherein various parameters are defined and a description of how to generate them is given. For example, paragraph 67 states, "Extracted structures typically refer to simplified or amplified representations of features derived from images. An example would be binary images of trabecular patterns generated by background subtraction and thresholding."

Example 1 also provides details of how parameters such as measurement of the femoral cortex, watershed segmentation for characterizing trabecular structure and biomechanical testing of femurs for fracture load, are obtained, and includes a discussion of the combination of image information.

Additional teachings are found in example 3, which details how information obtained by the disclosed and claimed method is used to determine the risk of sustaining a hip (or bone) fracture (i.e. a bone disease).

Therefore, Applicants believe they have sufficiently pointed out and distinctly claimed the subject matter regarded as the invention as required by 35 U.S.C. §112.

35 U.S.C. §101

Claims 1and 6-22 stand rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter because the claims do not transform underlying subject matter to a different state or thing, nor are they tied to a particular machine.

35 U.S.C. §101 states, "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof,

may obtain a patent therefore, subject to the conditions and requirements of this title." The Supreme Court reflected that "Congress intended statutory subject matter to "include anything under the sun that is made by man."" *Diamond v. Diehr,* 450 U.S. 175, 182 (1981). The Court went on to outline,

> *That a process may be patentable, irrespective of the particular form of the instrumentalities used, cannot be disputed.* . . . A process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing. *If new and useful, it is just as patentable as is a piece of machinery.*

Diamond v. Diehr, 450 U.S. 175, 182-184 (1981) (citing *Cochrane v. Deener,* 94 U.S. 780, 787-788 (1877) (emphasis added).

Although applicants contend that the claims as examined are patentable subject matter under Section 101 and the Supreme Court's analysis, Applicants have amended the claims to ensure that both aspects of the test for statutory subject matter cited by the examiner are met. In other words, as amended, all of the claims are "new and useful" processes that (1) are tied to another class of statutory subject matter (*i.e.*, a machine in the form of a computer) and (2) transform the underlying subject matter (*i.e.,* transform electronic image data into representations of risk of bone or articular disease).

Independent claim 1, as amended, is directed to patentable subject matter. Amended claim 1 meets both prongs of the test for patentability cited by the Examiner. First, claim 1 is a method of predicting bone or articular disease using a computer to electronically extract micro-structure from an electronic image and is thus tied to patentable subject matter. Second, claim 1 provides for combining determined parameters to predict the risk of bone or articular disease. In other words, amended claim 1 transforms parameters determined from an electronic image of a joint into representations of risk of bone or articular disease. Thus, claim 1 recites the transformation of "subject matter … to a different state or thing" which meets the test for patentability of a process as outlined by the Supreme Court in *Diamond v. Diehr.*

Claims 6-22 are dependent on claim 1 and are each patentable for the same reasons.

35 U.S.C. §102

Claims 1, 6-10 and 12-13 are rejected under 35 U.S.C. §102(b) as being anticipated by United States Patent 5,915,036 (Grunkin et al., hereinafter Grunkin).

Claim 1 defines, in relevant part, a method of predicting bone or articular disease that includes determining one or more micro-structural parameters, one or more macroanatomical parameters, and one or more biomechanical parameters of a joint. Once the parameters are determined, the method combines the parameters to predict the risk of bone or articular disease. The combined parameters include a microstructural parameter, a macro-anatomical parameter, and a biomechanical parameter.

Grunkin does not teach such a method. For example, Grunkin does not teach or suggest combining multiple parameters as disclosed and claimed, namely, a microstructural parameter, a macro-anatomical parameter, and a biomechanical parameter to predict the risk of bone or articular disease. Instead, Grunkin discloses methods based almost entirely on a single micro-structural parameter, trabecular structure. Grunkin discloses a method of estimating the bone quality of a vertebra using a two-dimensional image (See Grunkin, col. 3, lines 25-30). In particular, Grunkin performs at least one of a variety of background correction techniques and manipulates the two-dimensional image to either enhance prominent features or reduce less dominant features (See Grunkin, col. 4, lines 43-54). Grunkin then extracts information about the trabecular structure from the manipulated image and estimates the bone quality (See Grunkin, col. 4, lines 55-60). Grunkin extracts the trabecular information and then introduces the information into an estimation procedure.

Grunkin's method is in direct contrast to claim 1, which requires at least one each of a micro-structural, macro-anatomical, and biomechanical parameter to be combined in order to predict the risk of bone or articular disease.

The office action suggests that Grunkin teaches determining and combining the required parameters at column 4, lines 35-63. Applicants respectfully disagree. The cited passage describes using one parameter only, trabecular structure. It describes that Grunkin uses local image intensity information and variation in the local intensity to extract information relating to the trabecular structure and then uses an estimation procedure to estimate bone quality from the extracted information. The passage does not disclose claim 1 of the present application.

Although Grunkin suggests that other explanatory features (such as age, sex, species, race, and the specific bone considered in the vertebrae may be included in the estimation procedure), none of the other information constitutes, for example, a macro-anatomical parameter. The term macro-anatomical parameter refers to those parameters that may be measured on the macro-scale (e.g., using a ruler). Such parameters include, without limitation, the overall geometry of the bone, the length of the femoral neck, diameter of the femoral head, thickness of the cortical bone, etc.

Furthermore, Grunkin emphasizes in several parts of the specification that the trabecular structure is one of only a few relevant parameters, none of which are macro-anotomical. For example, in discussing the data presented at the end of the detailed description, Grunkin states that "the optimal fracture load of trabecular bone may be predicted using only textural parameters" and that "neither sex nor BMD can add information to the description." (see Grunkin at col. 35, lines 30-45.) Additionally, in analyzing study data presented in an example, Grunkin also states:

> Most of the explanatory effect is contained in the age and the sex. The rest of the variability (approximately 16% point) is explained by the textural features.

(see Grunkin at col. 24, lines 1-3.) The examples in Grunkin explicitly teach parameters that primarily rely on trabecular structure and that do not include the additional claimed types of parameters. Grunkin additionally teaches against the use of BMD, which the present specification includes as a useful parameter. Thus, although Grunkin does teach that additional "explanatory features" may be used, Grunkin does not disclose any macro-anatomical variables, and any biomechanical parameters appear to be derived from the trabecular structure.

Therefore, since Grunkin fails to teach or suggest determining and combining the parameters required by claim 1 (e.g., micro-structural, macroanatomical, and biomechanical), claim 1 is allowable over Grunkin. Moreover, claims 6-10, 12, and 13, which depend from claim 1, are allowable for at least the same reasons.

Claims 1 and 6-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al., U.S. Patent Number 6,442,287, (hereinafter Jiang).

Claim 1 defines, in relevant part, a method of predicting bone or articular disease that includes determining one or more micro-structural parameters, one or more macroanatomical parameters, and one or more biomechanical parameters of a joint. Once the parameters are

determined, the method combines the parameters to predict the risk of bone or articular disease. The combined parameters include a microstructural parameter, a macro-anatomical parameter, and a biomechanical parameter.

Jiang does not teach such a method. Instead, Jiang discloses an automated method, storage medium and system for analyzing bone wherein the strength of the bone is estimated based on bone mineral density and at least one of bone geometry, the Minkowski dimension and trabecular orientation. Stepwise regression and best subset selection are then used to select and merge the descriptors of bone mineral density and structural features into a single index, which is then evaluated as a predictor of biomechanical properties. (see Jiang at Col. 15, lines 24-28). In other words, two parameters are determined and merged into a single index which is then used to predict a third parameter (biomechanical properties), whereas claim 1 requires determining and combining micro-structural parameters, macroanatomical parameters and biomechanical parameters to predict the risk of bone or articular disease.

Therefore, since Jiang fails to teach or suggest determining and combining the parameters required by claim 1 (e.g., micro-structural, macroanatomical and biomechanical), claim 1 is allowable over Jiang. Moreover, claims 6-13, which depend from claim 1, are allowable for at least the same reasons.

35 U.S.C. §103(a)

Claim 11 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Grunkin in view of Jiang.

As a dependent claim of claim 1, claim 11 includes all of the limitations of independent claim 1, which is allowable over Grunkin and Jiang as discussed above. Therefore, claim 11 is also allowable over Grunkin and Jiang for at least the same reasons.

In addition, there is no motivation to combine Grunkin and Jiang, because Grunkin teaches against the use of principles fundamental to Jiang, namely the use of bone mineral density "BMD"). Grunkin includes a lengthy critique of prior uses of BMD throughout the opening "Background" section of the patent. (See, e.g., Grunkin, col. 1, line 1 to col. 3, line 21.) Furthermore, Grunkin expressly states that:

> It is obvious that BMD is not a significant feature and that it can be eliminated from the model. Using BMD as the only descriptive parameter, a multiple R-squared of R.sup.2 =0.2142 is obtained indicating that BMD is a poor indicator

> of the quality of trabecular bone. Thus, the aspects of fracture risk relating to trabecular bone are poorly described by BMD. (Grunkin, col. 34, lines 29-34.)

On the other hand, as stated in the Abstract and throughout the specification, Jiang teaches a method that relies on the use of BMD. It would not be obvious to one of skill in the art to combine a reference that relies on a principle, such as BMD, with another that harshly critiques the use of that principle.

Claims 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Number 6,306,822 (Kumagai et al., hereinafter Kumagai) in view of Grunkin. As dependent claims of claim 1, claims 14-19 include all of the limitations of claim 1. Therefore, claims 14-19 are allowable over Grunkin for at least the same reasons as discussed above for claim 1.

In addition, Kumagai fails to satisfy the deficiencies of Grunkin. In particular, Kumagai teaches a phosphopeptide and a method of treating bone disease using the phosphopeptide. Kumagai fails to teach or suggest determining and combining the parameters required by the present claims. Accordingly, Grunkin and Kumagai fail to teach or suggest, alone or in combination, all of the limitations of claims 14-19. Therefore, claims 14-19 are allowable over the combination of Grunkin and Kumagai.

Also, Kumagai measures bone mineral content, for example, in FIG. 3-5, to measure reductions in bone loss. Thus, as with Jiang, it would not be obvious to combine a reference that relies on bone mineral content with a reference that critiques the application of BMD – a closely related concept.

Claims 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grunkin. As dependent claims of claim 1, claims 20-22 include all of the limitations of claim 1. Accordingly, claims 20-22 are allowable over Grunkin for at least the same reasons as discussed above for claim 1.

The office action suggests that Grunkin does not specifically disclose the steps in which the parameters used are selected from the group consisting of total cartilage volume as claimed in claim 20 and from the group of a volume of bone marrow as claimed in claim 21. The office action further suggests that it would have been an obvious matter of design choice to modify the method of Grunkin by replacing the trabecular parameters with cartilage and bone marrow volume parameters to determine bone strength and fracture risk. However, there is no analysis

indicating why this would be true, and nothing in Grunkin suggests that trabecular structure is interchangeable with cartilage volume or bone marrow parameters.

Moreover, even if this were true, Grunkin still fails to teach or suggest determining one or more micro-structural parameters, macroanatomical parameters, and biomechanical parameters in a joint and combining the parameters (including a micro-structural parameter, a macro-anatomical parameter, and a biomechanical parameter) to predict the risk of bone or articular disease. Therefore, claims 20-22 are allowable over Grunkin for at least the same reasons as discussed above for claim 1.

CONCLUSION

It is believed that the application is now in order for allowance and Applicants respectfully request that a notice of allowance be issued. Applicants believe that a two month extension of time is required and hereby request that the associated fees be charged to Deposit Account No. 19-4972. Applicants also request that any other fee required for timely consideration of this application be charged to Deposit Account No. 19-4972. Applicants also request that the examiner contact applicant's attorney if it will assist in processing this application through issuance.

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Respectfully submitted,

/Jonathan C. Lovely, #60,821/
Jonathan C. Lovely
Registration No. 60,821
Attorney for Applicant

Sunstein, Kann, Murphy & Timbers LLP
125 Summer Street
Boston, MA 02110-1618
(617) 443-9292
03155/00121 1247950.1